REMARKS

Status of the Claims

The Examiner's acknowledgement of the election without traverse of Group IV (claims 10-15, 21, and 22) is recognized. Claims 1-9 and 16-20 are withdrawn from further consideration. Thus, claims 10-15 and 21-22 are under examination.

Claim Rejection - 35 U.S.C. §103

Claims 10-15, 21 and 22 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over U.S. Patent No. 6,866,849 (hereafter "the '849 patent") in view of Ghanta et al., 1996, *J. Biol. Chem.*, 271(47): 29,525-29,528 (hereafter "Ghanta"), U.S. patent no. 6, 962,707 (hereafter "the '707 patent"), and Maillere et al., 1995, *Molecular Immunology*, 32(17/18): 1377-1385 (hereafter "Maillere"). The Examiner states that these documents provide sufficient motivation to combine the teachings of the foregoing references to arrive at the claimed invention with a reasonable expectation of success, and that such a combination teaches each and every limitation of the claims. These grounds for rejection are not well taken and are respectfully traversed.

Obviousness requires that each and every claim limitation be disclosed or suggested by the prior art. The '849 patent, Ghanta, the '707 patent, and Maillere do not suggest, alone or in combination, the instant claims because they do not suggest the synthetic amyloid β (hereafter "Aβ") peptides defined by the claims nor that such claims are capable of eliciting a desired immune response.

At the outset, it should be noted that the claimed peptides must comprise an N-terminal and/or C-terminal polylysine or polyaspartate of 4-10 residues. On page 2, last sentence of the May 23, 2006 Office Action, the Examiner incorrectly states that the 4-10 lysine or aspartate residues at either end of the peptide is optional.

The pending claims are directed to Aβ peptides for use as an immunogen to mount an immune response designed to interfere with natural Aβ peptides and amyloid deposits. The

inventive peptides have reduced ability to adopt β-sheet conformation as an antigenic source and have a lower risk of leading to any toxic effects in humans. The peptides called for in the present claims are based upon SEQ ID NO: 1 with the modifications as described:

An isolated peptide comprising the amino acid sequence:

(Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala)$_n$ (SEQ ID NO:1)

wherein n is 1 or 2; and

an N-terminal, C-terminal, or both N- and C-terminal, polylysine or polyaspartate sequence of 4-10 residues.

The Examiner relies upon the '849 patent as the primary reference for his obviousness rejection. The '849 patent discloses administration of a peptide consisting of the first 39 amino acids of natural amyloid β (hereafter "Aβ1-39") for evoking a therapeutic antibody response. The Examiner acknowledges that the '849 patent is silent regarding any modifications to the natural Aβ1-39 fragment. Moreover, the '849 patent does not teach or suggest the synthetic Aβ peptides defined by the instant claims.

The Examiner attempts to cure the deficiencies of the '849 patent with Ghanta. However, nothing in Ghanta, alone or in combination with the '849 patent, suggests or teaches Applicants' peptides as defined by the present claims.

The claimed synthetic peptides comprise amino acids 1-30 of the N-terminus of the full length Aβ sequence. Ghanta does not disclose or suggest an N-terminal Aβ peptide as called for in the present claims. Instead, Ghanta teaches modification of a peptide consisting of amino acids from the interior of the full-length Aβ sequence. That is to say, the Ghanta peptides comprise amino acids from the internal (not the N-terminal or C-terminal) portion of the full length Aβ. These peptides were designed to act as inhibitors of Aβ toxicity by altering Aβ self-assembly. For example, in Figure 1 Ghanta describes an exemplary inhibitor peptide consisting of a recognition

element of internal amino acids 15-25 of Aβ (hereafter "Aβ15-25") with glycine spacers, an aminocaproate linker, and six lysine residues at the C-terminus of the internal amino acids Aβ15-25 sequence (referred to in Ghanta, and hereafter, as H2). In Figure 1, Ghanta describes another inhibitor consisting of a recognition element of internal amino acids Aβ15-25 with glycine spacers and six lysine residues at the N-terminus of the internal amino acids Aβ15-25 sequence (referred to in Ghanta as H1). Aβ peptide fragments comprising internal amino acids of full-length Aβ are not the same as fragments comprising the N-terminus of full length Aβ.

A skilled worker would not have been motivated by Ghanta's teachings (pertaining to an internal amino acid sequence) to prepare the peptide defined by the present claims, which has an amino acid sequence with elements that do not correspond to the sequences disclosed in Ghanta. Thus, the present claims call for an N-terminal Aβ1-30 fragment (either one fragment of 30 amino acids, or two fragments of 60 amino acids), and these sequences are not suggested or disclosed in Ghanta.

Ghanta does not teach or suggest using a different or longer sequence of amino acids from Aβ than the 10 amino acid fragments described as H1 and H2 . If anything, Ghanta states that shorter peptide sequences, D-amino acid sequences, or organic peptidomimetics could serve as recognition elements in place of Aβ15-25 (See Ghanta, page 29528, column 2). This is hardly a suggestion that would lead one of ordinary skill to create a longer peptide comprising the N-terminal of Aβ.

Additionally, Ghanta does not describe or suggest use of the inhibitor fragments as immunogens. A skilled worker would not have been motivated by an inhibitor consisting of an internal sequence of full length Aβ, to make or use the claimed peptides comprising the N-terminus of full length Aβ. Importantly, the skilled worker would have no reasonable expectation that an inhibitor may be used successfully as an immunogen. For this reason, and contrary to the Examiner's statement, a skilled worker would not reasonably expect that the net benefit of the combined methods of the '849 patent and Ghanta would be greater than that taught in the '849 patent. In fact, as discussed above, there would have been no motivation for a skilled worker to use

the inhibitor, as modified by Ghanta, as an immunogen to arrive at the present claims. Thus, Ghanta fails to cure the deficiencies of the '849 patent.

The Examiner cites the '707 patent as demonstrating the success a skilled worker would expect if he combined the teachings of the '849 patent with the teachings of Ghanta. The '707 patent discloses a therapeutic agent comprising polylysine or polyglutamic acid linked to the amino or carboxyl terminus of an immunogenic, natural Aβ peptide. The Examiner acknowledges that the '707 patent does not teach polyaspartate of the 4-10 amino acid limitations taught by Applicants. However, the Examiner concludes that the '707 patent indicates that the "addition of polyamino acids to Aβ peptide immunogen is potentially beneficial and at least feasible." Applicants respectfully disagree with the Examiner's statements regarding Applicants' invention in light of the '707 patent.

As discussed above, because neither the '849 patent nor Ghanta describes or suggests Applicants' claimed peptides, the '707 patent does not demonstrate the success a skilled worker would expect if he combined the '849 patent and Ghanta. For that matter, the '707 patent, when considered alone, does not render the claimed peptides obvious.

The Examiner cites Maillere as allegedly teaching that amidation of the C-terminus of an administered peptide decreases proteolytic degradation of peptides, thereby enhancing the capacity of the peptide to activate lymphocytes. Based upon Maillere, the Examiner states that this modification would have been obvious to a skilled worker considering administration of a peptide for any purpose. Applicants respectfully disagree.

Maillere describes only a general procedure for C-terminal amidation of a T cell epitope containing peptide. The Examiner's opinion that the modification disclosed by Maillere of a peptide for administration for any purpose is untenable. Maillere does not disclose the procedure of C-terminal amidation for use with Aβ peptides. Maillere does not remedy the deficient teachings in the '849 patent, Ghanta or the '707 patent and does not disclose or suggest the synthetic Aβ peptides presently claimed. Therefore, Maillere cannot render the presently claimed invention obvious.

Accordingly, based upon the references cited by the Examiner, an artisan of ordinary skill would not have been motivated to make the synthetic Aβ peptides called for in the present claims, nor would the skilled worker have a reasonable expectation that such peptides would be successful inducing an immune response to amyloid deposits. There is no suggestion in the prior art to combine these four references to make the synthetic Aβ peptides of the present claims. Both the motivation to combine the relevant elements and the suggestion of success must be found in the prior art to satisfy the requirements for maintaining an obviousness rejection. *In re The Dow Chemical Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988) ("[b]oth the suggestion and the expectation of success must be founded in the prior art, not in the applicant's disclosure"). While not all of the elements of the presently claimed peptides can be found in the cited references, finding various elements piecemeal in separate references is ***not*** sufficient motivation to combine them to arrive at a claimed invention. *In re Rouffet*, 47 USPQ2d 1453 (Fed. Cir. 1998) ("[T]he examiner must show reasons that the skilled artisan, *confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.*") (citations omitted, emphasis added).

In conclusion, nothing in the '849 patent, Ghanta, the '707 patent or Maillere describe or suggest, alone or in combination, the presently claimed N-terminal synthetic Aβ peptides that elicit a desired immune response. Applicants respectfully request that the Examiner reconsider and withdraw the obviousness rejections and allow claims 10-15, 21 and 22.

CONCLUSION

In view of the above remarks, it is respectfully requested that the application be reconsidered and that all pending claims be allowed and the case passed to issue. If there are any other issues remaining which the Examiner believes could be resolved through a Supplemental Response or an Examiner's Amendment, the Examiner is respectfully requested to contact the undersigned at the telephone number indicated below.

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Respectfully submitted,

By _____

S. Peter Ludwig
Registration No.: 25,351
DARBY & DARBY P.C.
P.O. Box 5257
New York, New York 10150-5257
(212) 527-7700
(212) 527-7701 (Fax)
Attorneys/Agents For Applicant